IDENTIFYING RISK FACTORS IN GLOBAL CORONAVIRUS CUMULATIVE CASE FATALITY IN THE ABSENCE OF VACCINATION

BY

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ABSTRACT

Although the roll out of coronavirus vaccination has commenced in some countries, coronavirus (COVID-19) continues to be a deadly disease for some people. The case fatality rate is not uniform across countries globally and this raises the question: why is it so? In view of this question, this study sought to identify risk factors in COVID-19 cumulative case fatality among countries in the absence of vaccination using data from international data bases. The data were analysed using multivariate logistic regression based on this author's adaption of Mosley and Chen's framework of analysing child survival. The results suggest that in the absence of vaccination, direct and indirect factors included in the analysis do not have statistically significant effect on the probability of having high cumulative COVID-19 fatality in a country after controlling for confounding factors in a country. In view of this, it appears that we still know little about the risk factors associated with high cumulative COVID-19 fatality rate at country level. The relevance of these results at individual level needs to be established by further research.

NTRODUCTION

Background and Statement of the Research Problem

Coronavirus (COVID-19) continues to be a deadly disease for some people. The rollout of vaccination to combat COVID-19 commenced in some countries after this study was initiated. Prior to the

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vaccination rollout, national governments adopted two approaches in combating the virus. (1) Curtailing the spread of infections through various levels of lockdown, screening, and testing for the virus in communities in the population and quarantining those testing positive but without symptoms, advocating social/physical distancing, wearing of face mask in public, promoting frequent handwashing or using hand sanitizers etc. (2) Management of those testing positive and showing symptoms through its health system so that they recover from the infections. These approaches are still in place with ongoing vaccination.

Despite these approaches and since vaccination rollout, infections as well as case fatality from COVID-19 have continued to increase globally. Data from the World Health Organisation (WHO) indicate that as of 16 November 2020, there were 58,968,188 confirmed cases of COVID-19 globally and the cumulative case fatality globally increased from 66,022 as of 30 March 2020 to 1,387,647 as of 16 November 2020. The case fatality rate is not uniform across countries globally. For example, computation by this author from the WHO data indicates that while the cumulative case fatality rate from COVID-19 as of 16 November 2020 was 37.9 per thousand reported confirmed cases in the U.K, it was 20.8 per thousand reported confirmed cases in Senegal. This appears to suggest that the probabilities of dying from COVID-19 among persons infected with the virus, are higher in some countries compared to others. This raises this question, why is this so? Although the probability of death is 1.0 for all humans i.e., every person will at some point die, the right to life is a basic human right and it is the collective responsibility of individuals and the state to prevent all forms of premature mortality due to all forms of communicable and non-communicable diseases, and injuries. COVID-19 – a communicable disease – may be construed in this context. According to the WHO, COVID-19 is a deadly among all age groups in the population particularly the elderly and those who have a pre-existing condition which includes high blood pressure, heart and lung problems, diabetes, obesity, or cancer at individual level (WHO: 2019a). It is on this basis that some of the variables included in the analysis were selected.

Study Objective

The overall objective of this study therefore was to identify risk factors in COVID-19 cumulative case fatality among countries in the absence of vaccination. Specifically, the study attempted to identify the factors associated with high probability of COVID-19 cumulative case fatality rate among countries (high defined as exceeding a specified threshold, as explained in the methods section below).

DATA AND LIMITATIONS

The primary sources of data for this study were the World Bank, the World Health Organisation, and the United Nations data bases for the relevant co-variates for the period 2017 or 2010-2020 depending on the nearest available data point. In cases where the value of the population or socio-economic indicator was not available for a country from the data bases mentioned above, other sources were used which consisted of the country's statistical website or other agencies providing such information. The COVID-19 figures were obtained from the WHO website.

As indicated above, there were few instances where there was departure from using the World Bank's and World Health Organisation's (WHO) data bases, this can be considered as one of the limitations of the study as different standards from those of the World Bank and World Health Organisation may have been used in deriving and collating such data. In some instances, the values of the population or socio-economic indicators were not available from any source for some countries/territories. These were treated as missing cases in the analysis where such cases arose. These limitations may have compromised the comparability of data across countries. It is unlikely that unavailability of recent data for all the variables included in the analysis would have compromised the results because: (1) it was not specifically selective of certain countries, (2) values of indicators rarely change dramatically from one year to the another.

METHODS

CONCEPTUAL FRAMEWORK FOR ANALYSIS

Mosley and Chen's (1984) conceptual framework for the study of child survival was adapted in identifying the risk factors in COVID-19 cumulative case fatality rate. The original framework by Mosley and Chen may be interpreted as stating child survival is a function of direct and indirect factors. According to the framework the indirect factors consist of socioeconomic factors but they operate through basic proximate (direct) factors that in turn influence the risk of disease and the outcome of diseases process. Although the original Mosely and Chen's framework was designed for child survival from all causes of morbidity and death, the perspective can be adapted for use to analyse, risk factors in COVID-19 fatality in this case, one cause of death and like the Mosely and Chen's framework, the risk factors in COVID-19 fatality may be classified into direct and indirect factors. Though not included in Mosley and Chen's framework of child survival in the adaptation, one also needs to take into consideration confounding factors. Though not the subject of this study, the adaptation of Mosely and Chen's framework can be suitably applied in the analysis of adult mortality. The factors in the current adaptation relevant to COVID-19 case fatality analysis were classified into three broad categories namely direct, indirect, and confounding factors. Within each category, the following factors were identified.

Direct (Proximate) Factors

Demographic factors: Age and sex. The primary focus in this study was the age composition of the population because the interest in this study was not differences in COVID-19 case fatality by sex at individual level. It has long been established in the demographic literature since the first life tables by John Graunt in 1662, that mortality in human populations portray an age pattern that is typically U – or J – shaped irrespective of levels of mortality in the absence of HIV/AIDS. Age patterns of mortality usually exhibit high rates in infancy or childhood and increasing rates over age 50 (see for example Heligman and Pollard, 1980; United Nations (UN), 1982; Coale and Demeny 1983). With HIV/AIDS, the age pattern of mortality exhibits a characteristic hump in young adult ages due to increased AIDS related deaths in these ages (see INDEPTH Network 2004). While some populations in the world may be described as ageing populations due to high proportions of the elderly, some populations are "young" especially in many African countries. The distribution of diseases and disease-type is different across age groups. For instance, degenerative non-communicable diseases are prevalent among the elderly (Gyasi and Phillips (2020). A summary measure of the ageing of population is the median age. According to Shryock, Siegel and Associates (1976), a population may be described as young if the median age of the population is under 20 years, intermediate if the median age is 20-29 years, and old if the median is 30 years or over. It follows from the above therefore that the age composition of the population needs to be taken into consideration in any comparative analysis of COVID-19 case fatality among different countries.

Illness control: This component relates to medical treatment and measures taken to cure diseases after they become manifest (Mosley and Chen, 1984). The quality of the health care system and access to medical care in populations are important considerations in analysing the outcome of a disease. Kobewka, Walraven, Turnbull et al. (2017) have observed that increased mortality rate can be caused by poor quality health care. Indicators of health care quality may include number of health personnel (doctors) per thousand population, number of beds per thousand population. Access indicator may include percent of population with access to health facility or index of universal health access. Index of universal health access though does not capture all the dimensions of illness control was used in this study due to data constraint. The index captures essential health service coverage without financial hardship and its value ranges between a unitless scale of 0 to 100. A value of 100 implies everyone in the population has access to essential health service without financial hardship (WHO 2019b).

Indirect (Socioeconomic) Factors:

Level of Economic Development: There is a two-way relationship between level of economic development. Avoidable deaths result in economic losses in the form of decline in GDP (Alkire et al. 2018) cited in Stefko, Gavurora, Ivankova et al. (2020). Chung, Schooling, Cowling et al.'s (2010) study in China showed that economic development and the correspondingly improved nutrition, living conditions, and medical care were generally associated with decreasing mortality. Indicators of level of economic development may include per capita GDP, percent of GDP spent on health sector (i.e. health financing). Nominal GDP per capita was utilised in this study.

Environment: Access to Adequate drinking water: In the original Mosley and Chen's framework, environmental contamination is treated as direct factor in child survival however since unsafe water is the relevant environmental factor of interest in the current study, it is treated as an indirect factor. Thus, environmental factors could be a direct or indirect factor depending on the indicator chosen. Unsafe drinking can be a major cause of death (Kim, Cheong, and Jeon, 2018). Although unsafe water may be related to handwashing, it is unlikely however that it would result in immediate cause of death. Water borne disease outbreaks are associated with occasionally high levels of mortality (Ligon and Bartram, 2016). The indicator of adequate access to drinking water used in this study was percent of the population using at least basic drinking water services.

Behavioural: At an aggregate level, behavioural factors relevant to this study include the prevalence of smoking and alcohol consumption in the population. Smoking generally increases the risk of mortality but it is not clear how the relative risk varies by cause of death (Taghizadeh, Vonk and Boezem 2016). According to Degerud, Ariansen, Ystrom et al. (2018), alcohol has multiple biological effects on the cardiovascular system, both potentially harmful and protective. Unfortunately, data on alcohol consumption could not be sourced.

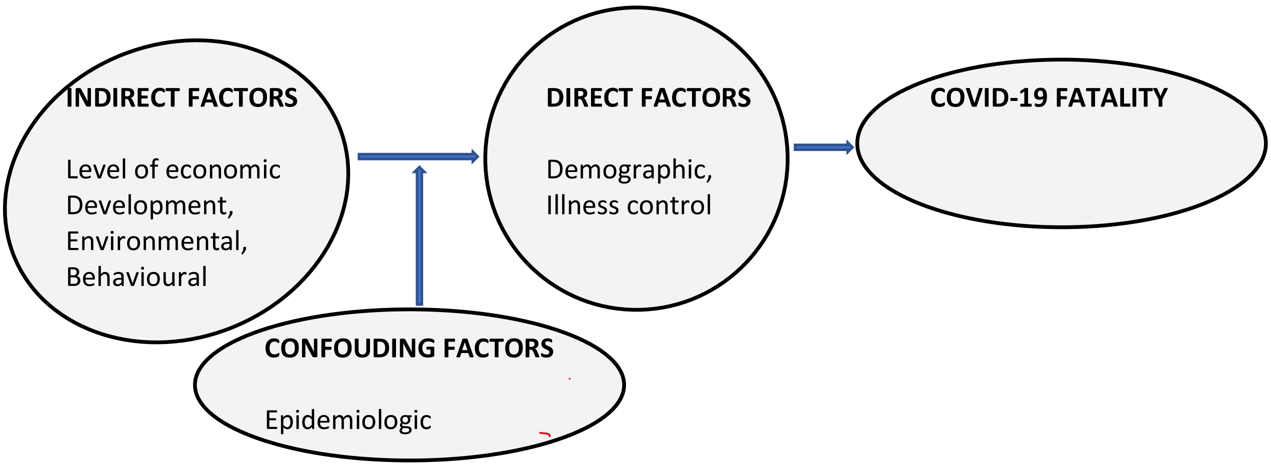
Confounders

In addition to proximate and indirect factors, it was necessary also to take into consideration confounding factors. As indicated above, the WHO (2019a). has identified existing condition which includes high blood pressure, heart and lung problems, diabetes, obesity, or cancer at individual level. Additionally, the confounders included in the analysis were based on the following considerations.

Epidemiological Factors: This relates to the prevalence of underlying medical conditions (or co-morbidity) in the population such as obesity, diabetes, HIV/AIDS, hypentension. Vidra, Bijlsma, Trias-Llimos et al. (2018) have noted that obesity increases the risk of a range of diseases as observed by Field et al. (2001) cited in Vidra, Bijlsma, Trias-Llimos et al. (2018) and consequently the risk of dying according to Global BMI Mortality Collaboration 2016 cited in Vidra, Bijlsma, Trias-Llimos et al. (2018). According to Raghavan, Vassy, Ho, et al (2019), diabetes mellitus is a risk factor for cardiovascular disease and has been associated with 2- to 4-fold higher mortality. Hongjuin (2013) has noted that lungs are the most involved organ by HIV/AIDS related diseases, and pulmonary infections are the main reasons for the increasing death rate from AIDS. Rodriguez-Iturbe, Pons and Johnson observed that hypertension occurs in about 23-43% of the world population aged 18 years and over and is the leading modifiable risk factor of death resulting from cardiovascular disease. Unfortunately, data on HIV/AIDS could not be sourced and was therefore not included in the analysis.

A diagrammatical representation summarising the conceptual framework is shown in Figure 1 below.

Figure 1: Conceptual Analytical Framework



Source: Author’s adaptation of Mosley and Chen’s framework.

THE STATISTICAL ANALYSIS MODEL

The statistical analysis in this study was carried out in three stages. Firstly, differences in the levels of cumulative case fatality rate from COVID19 among countries globally was established by: (a) Bar chart plot of cumulative case fatality rate sorted in ascending order by countries according to the values of cumulative case fatality rate; (b) from a frequency distribution of the case fatality rates, the mean, standard deviation, range, and median values of the cumulative case fatality rates were estimated. Secondly for each country for which the data were available, a bivariate scatter plot of COVID-19 cumulative case fatality rates (dependent variable) against each of the values of the direct, indirect, and confounding factors (independent variables) was done to examine visually, the relationship if any between the independent variables and cumulative case fatality rates. From the results, it was established that a linear regression model, even after some of the independent factors were transformed, did not adequately describe the relationship between COVID-19 cumulative fatality rates and each of the independent factors. As illustrated in Appendices 1a – 1c for example, the relationship is non-linear. A non-linear model was therefore required. A multiple logistic regression was chosen.

The multiple logistic regression consisted of several models in line with the conceptual framework outlined above. The first model without controlling for any factor, tested that the probability of a country having high cumulative COVID-19 fatality rate is time dependent i.e., the level of cumulative COVID-19 fatality rate in a country depends on the duration since the first case of COVID-19 in the country. The second model then regressed cumulative COVID-19 case fatality rates on proximate factors (demographic and illness control factors) controlling for duration since first case of COVID-19 in each country. The third model regressed cumulative COVID-19 case fatality rates on indirect factors (level of economic development, environmental and behavioural factors) controlling for duration since first case of COVID-19 in each country. The fourth model regressed cumulative COVID-19 case fatality rates on the proximate and indirect factors controlling for confounders (epidemiological factors) as well as duration since first case of COVID-19 in each country. Because values of some the indicators were not available for some countries and to reduce the number empty cells in the multiple classifications of variables in the multivariate analysis, the logistic regression models entailed classifying the dependent and independent variables as dichotomous variables. The logistic regression model thus, estimated the probability that a country's cumulative case fatality rate per 1,000 above the 75-percentile value for all countries as of 16 November 2020, is associated with the country's direct or indirect factors' median values exceeding the 75-percentile value for all countries for the direct or indirect factors controlling for confounders at or close to the specified date of the dependent variable.

It may be argued that the selection of any threshold (in this case, 75-percentile) is subjective. To avoid subjectivity in the selection, the following were considered. The 50 percentile which is equivalent to the median simply splits the distribution of the cases (the countries) into two equal halves regarding any indicator, thus does not provide disparities among countries regarding any indicator. Although the 70-percentile provided some disparities, the 75-percentile provided better disparities and without having to few cases at one end and too many cases at the other hand which would have been the case if a higher than 75-percentile were used in the analysis.

The general form of the logistic regression equation was based on Hosmer and Lemesho (2000) expressed as:

The logistic regression equation is:

$$Prob(CFR) = \frac{1}{1+ e^{-(B_0+ B_1X_1+ \ldots +B_n X_n)}}.$$

Prob(CFR) – the dependent variable - is the probability of a country having COVID-19 cumulative case fatality rate percentile value for all countries or higher as of 16 November 2020. The specified date was to avoid the complicating effects of COVID-19 vaccine uptake although though this started in many countries in early 2021.

For each country, the dependent was coded 0, if the cumulative case fatality rate per 1,000 confirmed cases was below the 75-percentile value for all countries for which data were available i.e., low cumulative case fatality rate, and 1, if the cumulative case fatality rate was the same or higher than the 75-percentile value for all countries i.e., high cumulative case fatality rate. The direct, indirect, and confounding factors (independent variables) were similarly coded into low and high depending on their 75-percentile values. Although high or low were classificatory outcomes, they were quantitatively defined as seen from above. The meanings of the other terms in the in the equation are:

e = base of the natural logarithm.

β_0 = constant.

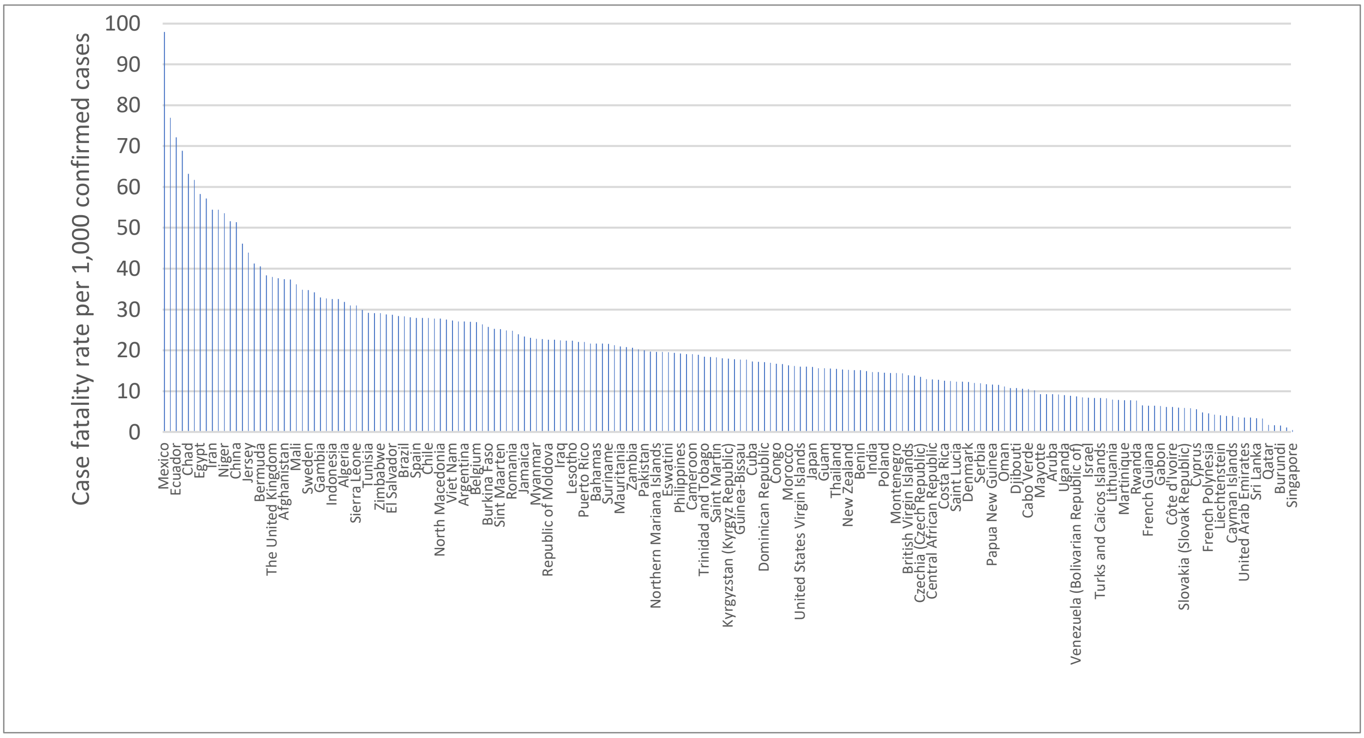
$\beta_{1..n}$ = estimated coefficients corresponding to the covariates $X_1 \ldots X_n$.

RESULTS

Levels of Coronavirus Cumulative Case Fatality Rates globally

Figures 2 shows the levels in cumulative case fatality rates globally as of 16 November 2020. The rates per 1,000 confirmed coronavirus cases ranged between 0.48 (Singapore) and 97.9 (Mexico). The distribution of the cumulative case fatality rates per 1,000 confirmed cases depicted in Figure 2 has a mean value = 21.1, Standard Deviation= 15.3 and Median = 18.0.

Figure 2: Global COVID-19 Cumulative Case Fatality Rates as of 16 November 2020 in the Absence of Vaccination



Source: Author's graph from WHO figures.

Table 1 summarises the 50-percentile and 75-percentile distributions of the values of the independent variables among the 189 countries/territories analysed for which data were available. The 50-

percetile is the median value that splits all countries into two equal halves while the 75-percentile is the value in which 75% of countries have values less than or equal to the 75-percentile. As an example, in 2019, the median age of the population for all countries ranged between 15.15 years (Niger) and 48.36 years (Japan) resulting in a 50-percentile (median) value of 30.73 years and 75-percentile value of 39.84 years. The 50-percentile and 75-percentile values of the other factors shown in Table 1 have similar interpretation though the reference dates are not the same. As noted earlier, this study was initiated before vaccine rollout in any country hence the data utilised do not capture the possible impact of vaccination on COVID-19 fatality.

Table 1: Summary indicator Values of Risk Factors for all Countries with Data in the Absence of Vaccination (number of countries/territories = 189)

Indicators	Median Value (50 Percentile value)	75-percentile Value
Dependent Variable:		
Cumulative case fatality rate per1,000 confirmed cases (16 Nov 2020)	17.96	27.63
Proximate Risk Factors:		
Median age of population (years, 2019)	30.73	39.84
Percent of Population 60 years and over (2019)	11.64	22.09
Index of universal health access (2015)	0.64	0.75
Indirect Risk Factors		
Nominal GDP per capita US$ (2017)	7,495.50	25,166.00
Percent of population using at least basic drinking water Services (2016)	88.81	98.76
Prevalence of daily smoking (Persons 15 years and over, 2010)	18.30	23.35
Confounding Risk Factors		
Prevalence of obesity (adults 20 years and over, 2016)	19.1	25.65
Prevalence of raised blood glucose (Persons 18 years and over, 2014)	7.40	9.90
Prevalence of raised blood pressure (Persons 18 years and over, 2014)	23.30	27.80
Time Since Infection up to 16 November 2020		
Days since first confirmed case	253	262

Source: Author's computations from international data bases.

Table 2 shows the summary ranking of countries/territories in the levels of the indicators included in this study. The available data from the international data bases at the time of the study suggest that of Japan, Italy, and Martinique had the highest median age of the population in that order in 2019 while Niger, Mali and Chad in that order had the lowest median age of the population in the same period. The countries shown corresponding to the other indicators have similar interpretation though the reference dates differ.

Table 2: Summary Ranking in the Levels of Indicators in the Absence of Vaccination (number of countries = 189)

Indicators	Top 3 Countries/ Territories	Bottom 3 Countries/ Territories
Dependent Variable:		
Case fatality rate per1,000 confirmed cases	Mexico, Monsterrat, Ecuador	Singapore, Gibralter, Burundi
Proximate Risk Factors:		
Median age of population (years)	Japan, Italy, Martinique	Niger, Mali, Chad
Percent of Population 60 years and over	Japan, Italy, Portugal	UAE, Zambia, Qatar
Index of universal health access	Canada, Australia, Norway	Somalia, Madagascar, Chad
Indirect Risk Factors		
Nominal GDP per capita US$	Liechtenstein, Monaco, Luxembourg	Somalia, South Sudan, Burundi
Percent of population using at least basic drinking water services	Australia, Singapore, New Zealand +	DRC, Angola, Somalia
Prevalence of daily smoking (Persons 15 years and over)	Greece, Serbia, Bosnia & Herzegovina	Ethopia, Ghana, Panama
Confounding Risk Factors		
Prevalence of obesity (adults 20 years and over)	U.S.A, Kuwait, Saudi Arabia	Burundi, Vietnam, Timor-Leste
Prevalence of raised blood glucose (Persons 18 years and over)	Kuwait, Qatar, Egypt	Switzerland, Burundi, Denmark
Prevalence of raised blood pressure (Persons 18 years and over)	Niger, Somalia, Chad	USA, Canada, Peru
Time Since Infection up to 16 November 2020		
Days since first confirmed case		

Sources: Author's ranking based on figures in international data bases.

Bi-Variate Analysis Results

Table 3 summarises the results of the bi-variate logistic regression of cumulative COVID-19 case fatality rate on each of the direct, indirect, and confounding variables.

Table 3: Bi-variate Regression of COVID-19 Fatality rate and Covariates in the Absence of Vaccination (number of countries/territories = 189)

COVID-19 Fatality rate regressed on			
Covariates	**Coefficient**	**Standard Error**	**Significance**
Days since first confirmed case >= 262 days (high) < 262 days (low) (RF)	0.322	0.368	0.381
Median age of population (years) >= 39.84 years (high) < 39.84 years (low) (RF)	-0.764	0.484	0.114
Percent of Population 60 years and over >= 22.1 (high) < 22.1 (low) (RF)	-0.764	0.484	0.114
Index of universal health access >= 0.75 (high) < 0.75 (low) (RF)	0.649	0.385	0.092
Nominal GDP per capita US$ >= 25,166 (high) < 25,166 (low) (RF)	-0.001	0.388	0.998
Percent population using at least basic water services >= 98.76 (high) < 98.76 (low) (RF)	-0.475	0.425	0.263
Prevalence of daily smoking >= 23.35 (high) < 23.35 (low) (RF)	-0.185	-0.525	0.725
Prevalence of obesity >= 25.65 (high) < 25.65 (low) (RF)	0.197	0.394	0.617
Prevalence of raised blood glucose >= 9.9 (high) < 9.9 (low) (RF)	0.501	0.386	0.195
Prevalence of raised blood pressure >= 27.8 (high) < 27.8 (low) (RF)	-0.291	0.415	0.484

Source: Author's computations from International data bases. RF = Reference category.

Table 4: Multi-variate Regression of COVID-19 Fatality rate and Covariates in the Absence of Vaccination (number of countries = 189)

COVID-19 Fatality rate regressed on						
	Model 1 (Proximate Factors)		Model 2 (Indirect Factors)		Model 3 (Full model)	
Covariates	**Coefficient**	**Odds Ratio**	**Coefficient**	**Odds Ratio**	**Coefficient**	**Odds Ratio**
Days since first confirmed case >= 262 days (high) < 262 days (low) (RF)	0.073 (0.448)	1.076	0.175 (0.508)	1.192	0.127 (0.541)	1.136
Median age of population (years) >= 39.84 years (high) < 39.84 years (low) (RF)	-1.116 (0.559)*	0.328			-1.250 (0.660)	0.287
Percent of Population 60 years and over >= 22.1 (high) < 22.1 (low) (RF)						
Index of universal health access >= 0.75 (high) < 0.75 (low) (RF)	1.008 (0.451)*	2.739			1.208 (693)	3.340
Nominal GDP per capita US$ >= 25,166 (high) < 25,166 (low) (RF)			1.403 (0.912)	4.067	0.298 (0.795)	1.347
Percent population using at least basic water services >= 98.76 (high) < 98.76 (low) (RF)			-1.428 (0.847)	0.240		
Prevalence of daily smoking >= 23.35 (high) < 23.35 (low) (RF)			0.072 (0.553)	1.074	0.385 (0.662)	1.470
Prevalence of obesity >= 25.65 (high) < 25.65 (low) (RF)					0.203 (0.559)	1.225
Prevalence of raised blood glucose >= 9.9 (high) < 9.9 (low) (RF)					0.318 (0.638)	1.374
Prevalence of raised blood pressure >= 27.8 (high) < 27.8 (low) (RF)					0.625 (0.658)	1.868
Constant	-1.260		-1.139		-1.775	
Nagelkerk R^2	0.067		0.053		0.093	

Source: Author's computations from International data bases. Standard errors in parenthesis.
* Statistically significant at $p < 0.05$. RF = Reference category.

The results were mixed. In the absence of vaccination, the bi-variate results suggest that without controlling for other factors, there is a statistically non-significant positive effect of long duration since the first confirmed case of COVID-19 in a country on the probability of having a high COVID-19 fatality rate in a country ($p > 0.05$). The results in Table 3 also suggest similar positive relationship between high cumulative case fatality rate in a country and high index of universal health access, high prevalence of obesity and high prevalence of raised blood pressure in a country without controlling for other factors but these relationships were also statistically non-significant ($p > 0.05$). However, the bi-variate results in Table 3 also suggest that without controlling for other factors and in the absence of vaccination, there is a negative but not statistically significant effect of high median age of the population, high nominal GDP per capita, high percentage of the population using at least basic water services, high percentage of the adult population smoking, high prevalence of raised blood pressure in a country on the probability of having a high cumulative COVID-19 fatality rate in a country ($p > 0.05$). The direction of the relationship regarding ageing of the population, access to health care, access to basic water services and prevalence of daily smoking appears counter intuitive. This necessitated further analysis in multivariate modelling controlling for other factors. The results are summarised in Table 4. The correlation Matrix showed that basic drinking water was highly correlated with GDP hence basic drinking water was dropped in the full multivariate model.

Controlling for proximate, indirect, and confounding factors, and in the absence of vaccination, the direction of the relationships between these factors in a country and the probability of having high COVID-19 fatality rate in a country in the bi-variate analysis remained the same as seen in Model 3, Table 4 in the multivariate analysis. Furthermore, the effects of these factors on the probability of having high cumulative COVID-19 fatality rate in a country were not significant in the full multivariate model ($p > 0.05$).

The odds ratios in Model 3 Table 4 suggest that after controlling for all other factors shown in the table, the odds of having a high cumulative COVID-19 fatality rate was less by about 71% in countries with high median age of the population compared with countries with low median age of the population though the difference was not statistically significant ($p > 0.05$). Furthermore, controlling for all other factors, the odds of having a high cumulative COVID-19 fatality rate was higher in countries with high index of universal access, high nominal GDP per capita, high prevalence of daily smoking, high prevalence of obesity, high prevalence of raised blood glucose, and high prevalence of raised blood pressure compared with countries with low values of these indicators. The differences were however not statistically significant ($p > 0.05$).

DISCUSSION AND CONCLUSION

According to the WHO (2021), older people, and those with underlying medical problems such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness if infected with COVID-19. The implication might be that at individual level, these group of people may have higher risk of fatality from COVID-19 if infected with the virus although the WHO does not make such claim. Using the World Bank, the World Health Organisation, and the United Nations data bases as the primary sources of data, this study sought to identify risk factors associated with high probability of cumulative COVID-19 fatality at country level in the absence of vaccination using Mosley and Chen's (1984) conceptual framework with some modification. Certain limitations in the study need to be noted. Some of the data are old. For example, the latest available data for raised high blood pressure was for the year 2014. The values of some of the indicators were not available for some countries/territories from any source. It is doubtful however, that more recent data if available would have changed the direction of the results.

Despite these limitations, the results from the analysis appear to suggest that in the absence of vaccination, selected direct (population ageing, access to health care) and indirect (GDP per capita, percent of the population using at least basic drinking water, prevalence of smoking) factors do not have statistically significant effect on the probability of having high cumulative COVID-19 fatality in a country after controlling for confounding factors (prevalence of obesity, prevalence of raised blood glucose, prevalence of raised blood pressure) in a country.

The Nagelkerk R^2 of the full multivariate model was only 0.093 which suggests one of, or all the following. (1) Some of the factors in the model may not be important risk factors in COVID-19 fatality at country level in the absence of vaccination. (2) The quality of the data in the measurement of the indicators in the dependent variable and co-variates may be poor in some countries relative to other countries, thus resulting in spurious relationships between the dependent variable and co-variates. For example, regarding the dependent variable in the current study, "Coverage and efficiency in screening and testing for COVID-19 as well as in the determination of cause of death would vary from country to country, thus global figures on confirmed COVID-19 cases as well as the number of COVID-19 fatalities are likely to be under-stated at any point in time" (Udjo 2020). (3) We still know little about the risk factors associated with high cumulative COVID-19 fatality rate at country level. Confounding factors such as obesity, raised blood sugar glucose, raised blood pressure as significant risk factors at country level in the absence of vaccination were not confirmed by this study. This raises the question: to what extent are these results relevant at individual level? This study was well underway before the development and rollout of COVID-19 vaccination. One may therefore also ask: will vaccination reduce differences in cumulative COVID-19 fatality rate among countries? Further research required to answer these questions.

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REFERENCES

Alkire, B.C., Peters A.W., Shrime M.G., et al., 2018. The economic consequences of mortality amenable to high-quality health care in low-and middle-income countries. *Health Affairs*, 37:988–996. doi: 10.1377/hlthaff.2017.1233.

Coale, A.J., and Demeny, P., 1983. Regional model life tables and stable populations. London: Academic Press.

Degerud, E., Ariansen, I., Ystrom, E., 2018. Life course socioeconomic position, alcohol drinking patterns in midlife, and cardiovascular mortality: analysis of Norwegian population-based health surveys. *PLoS Medicine,* 15 (1): e1002476.

Chung, R.Y., Schooling, C.M., Cowling, B.J., et al., 2010. How does socioeconomic development affect risk of mortality? An age-period-cohort analysis from a recently transitioned population in China. American Journal of Epidemiology, 171 (3): 345-356.

Gyasi, R.M., Phillips, D.R., 2020. Ageing and the rising burden of non-communicable diseases in sub-Saharan Africa and other low- and middle- income countries: A call for holistic action. The Gerontologist, Volume 60, Issue 5, August 2020, Pages 806–811, https://doi.org/10.1093/geront/gnz102

Heligman, L., and Pollard, J., 1980. The age pattern of mortality. Journal of the Institute of Actuaries, 107(1): 49-80. Doi: 10.1017/S0020268100040257.

Hongjun, L., 2013. HIV/AIDS related respiratory diseases. Radiology of HIV/AIDS, 30: 377-535.

INDEPTH Network, 2004. INDEPTH model life tables for sub-Saharan Africa. England: Ashgate Publishing Company.

Kim, J., Cheong, H., and Jeon, B., 2018. Burden of disease attributable to indadequate drinking water, sanitation and hygiene in Korea. Journal of Korean Medical Science, 33 (46): e288.

Ligon, G., and Bartram, J., 2016. Literature review of associations among attributes of reported water disease outbreaks. International Journal of Environmental Research and Public Health, 13 (6): 527.

Kobewka, D.M., van Walraven, C., Turnbull, J., et al., 2017. Quality gaps identified through mortality review. *BMJ Quality & Safety*, 26: 141-149.

Mosley, W.H., and Chen, L.C., 1984. An analytical framework for the study of child survival in developing countries. *Population and Development Review*, Supplement to Vol. 10: 25-48.

Raghavan, S., Vassy, J.L., Ho, Y., et al., 2019. Diabetes mellitus-related all cause and cardiovascular mortality in a national cohort of adults. *Journal of the American Heart Association*, 8 (4): e011295.

Rodriguez-Iturbe, B., Pons, H. and Johnson, R.J., 2017. Role of immune system in hypertension. *Physiological Reviews*, 97 (3): 1127-1164.

Shryock, H.S., Siegel, J.S., and Associates, 1976. The methods and materials of demography. New York: Academic Press, p. 132.

Stefko, R., Gavurora, B., Ivankova, V., et al., 2020. Gender inequalities and their effect on the economic prosperity represented by the GDP of selected developed countries – empirical study. *International Journal of Environmental Research and Public Health, 17 (10): 3555.* doi: 10.3390/ijerph17103555.

Taghizadeh, N., Vonk, J., and Boezem, M., 2016. Lifetime smoking history and cause-specific mortality in a cohort study with 43 years of follow-up. *PLoS One*, 11 (4): e0153310.

Udjo, E. O, 2020. Modelling coronavirus infections progression in South Africa. Available at: https://www.ericudjoconsulting.co.za/works/modelling-corona-virus-infections-progression-in-south-africa/. Accessed 27 May 2021.

UN, 1982. Model life tables for developing countries. New York: UN.

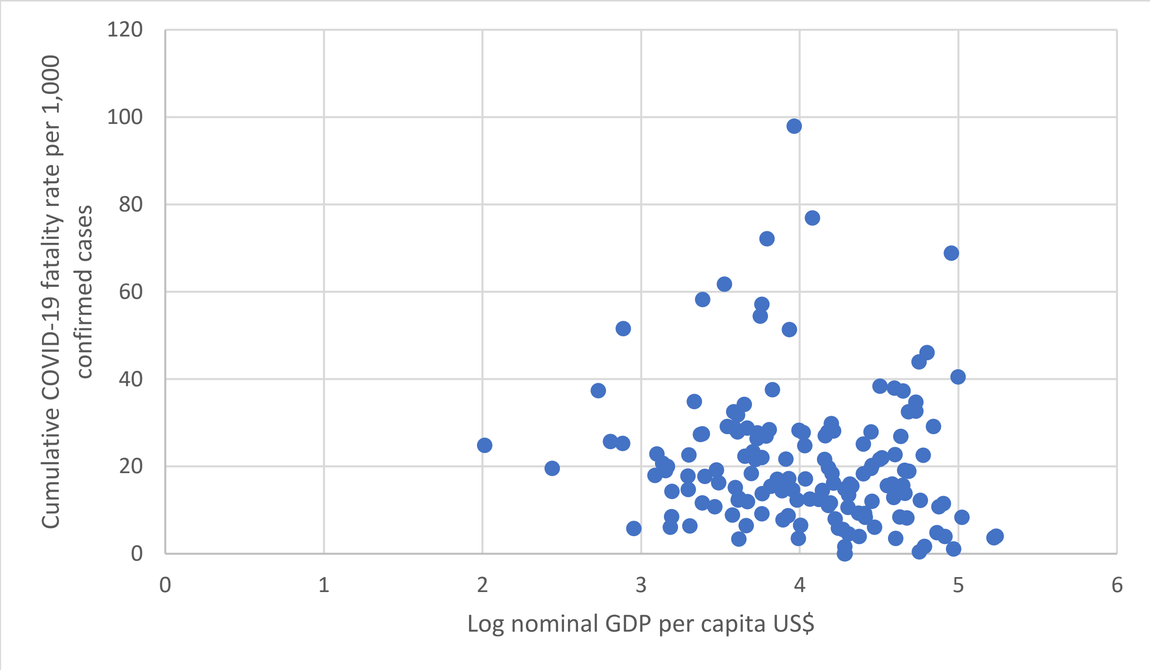
Vidra, N., Bijlsma, M.J., Trias-Llimos, S. et al. 2018. Past trends in obesity-attributable mortality in eight European countries: an application of age-period-cohort analysis. *International Journal of Public Health* 63 (6):683-692.

WHO, 2019a, Q & A on coronaviruses (Convid-19). Available on Coronavirus disease (COVID-19) (who.int)

WHO, 2019b. Index of universal health coverage 2015. Available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/uhc-index-of-service-coverage. Accessed 13 January 2021.

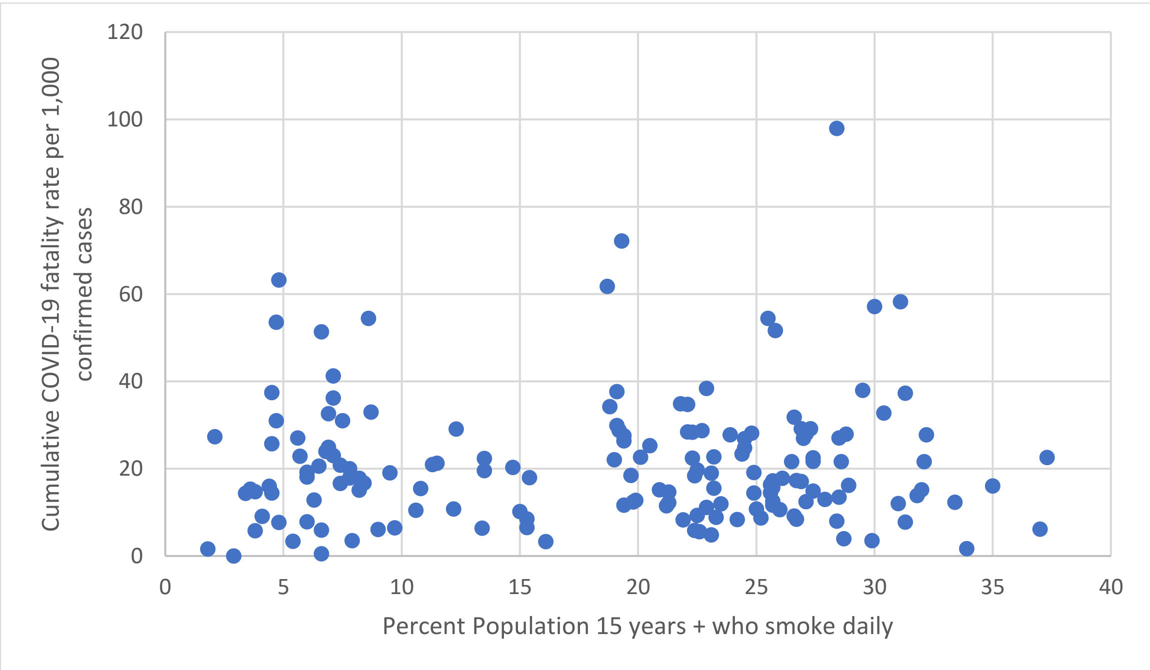
WHO, 2021. Coronavirus. Available at: https://www.who.int/health-topics/coronavirus#tab=tab_1. Accessed 27 May 2021.

APPENDIX 1A: Cumulative COVID-19 fatality rates and nominal GDP per capita



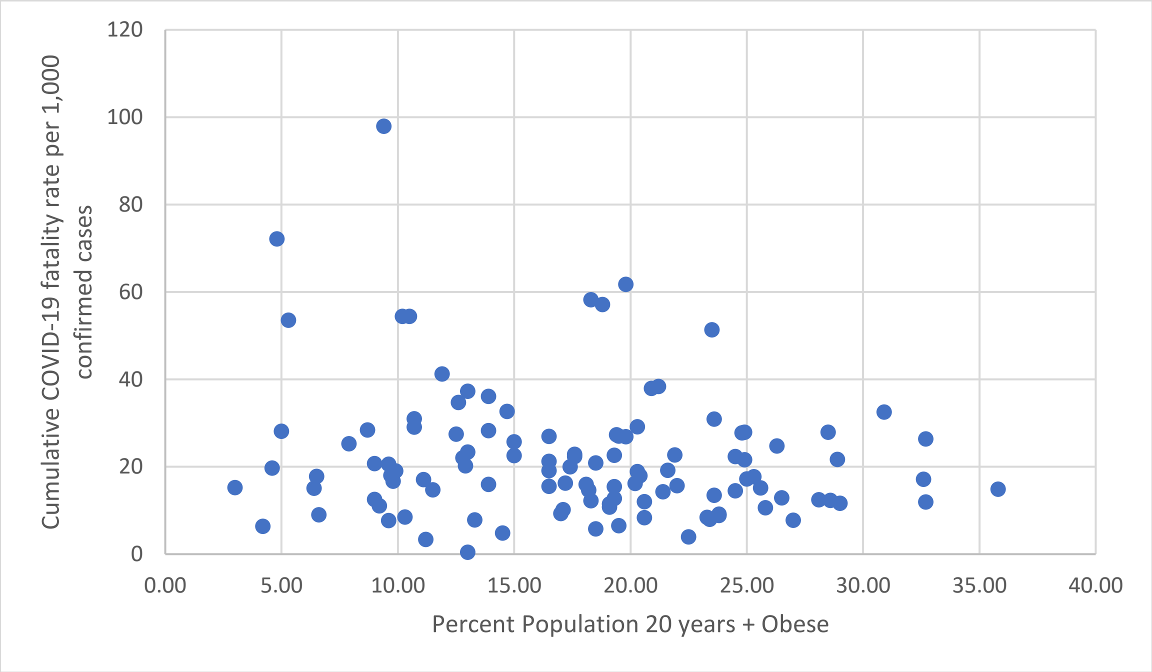
Source: Author’s graph from UN data.

APPENDIX 1b: Cumulative COVID-19 fatality rates and Obesity



Source: Author’s graph from WHO data.

APPENDIX 1c: Cumulative COVID-19 fatality rates and daily smoking



Source: Author's graph from WHO data.